National Institute of Allergy and Infectious Diseases / Division of Microbiology and Infectious Diseases	**Policy** Clinical Quality Management Plan	No.: DMID.OP.QMP001
	Approved: March 23, 2009 Effective Date: April 1, 2009	Version: 3.0

1.0 Purpose

The purpose of this policy is to describe the requirements for the development, implementation and evaluation of a Clinical Quality Management Plan (CQMP) for sites conducting Division of Microbiology and Infectious Diseases (DMID)-supported clinical research.

This policy lists *basic requirements* necessary for sites to comply with applicable federal and state regulations including protections of human subjects, International Conference on Harmonization (ICH) E6 Good Clinical Practice (GCP) guidance, the National Institute of Allergies and Infectious Diseases (NIAID) Clinical Research Standards, and NIAID Clinical Terms of Award.

2.0 Scope

This policy and applicable procedures apply to clinical research sites conducting DMID-supported clinical research.

DMID may request a copy of a site or protocol-specific CQMP for review and acceptance. For many sites, written agreements with DMID require sites / principal investigators to proactively submit clinical quality management plans for review and acceptance by DMID. For other sites, DMID may request a copy of a site or protocol-specific CQMP for review and acceptance, as DMID deems appropriate.

DMID reserves the right to review site CQMP findings.

3.0 Background

The CQMP policy describes elements to assist sites, conducting DMID-supported clinical research, with developing, implementing and evaluating such a plan. The CQMP should be easy to implement and serve as an on-site management tool to *internally* evaluate and document site performance of the protocol procedures, enable site staff to ensure that the rights and safety of human subjects are protected, and verify the data collected are accurate and complete throughout the implementation of the protocol. DMID makes available through the NIAID public website adaptable sample quality management plan templates and tools to meet the specific site/protocol needs. (http://www3.niaid.nih.gov/research/resources/DMIDClinRsrch/quality.htm)

Quality Management (QM) is an overall system of oversight to document and track site performance of DMID-supported clinical research. The QM activities facilitate planning for effective protocol implementation, ensure compliance with DMID requirements, identify areas in need of corrective action, verify the accuracy of data, and promote a constant state of readiness for an external audit or clinical monitoring visit.

The QM system includes Quality Control (QC) and Quality Assurance (QA). The focus is to provide site staff with the means to proactively identify and resolve problems with protocol implementation and regulatory compliance, *in the early stages*.

4.0 Definitions

- Clinical Research: Per the NIAID definition, patient-oriented research, including epidemiologic and behavioral studies, outcomes research, and health services research; research on mechanisms of human disease, therapeutic interventions, clinical trials, and development of new technologies, not including in-vitro studies using human tissues not linked to a living individual.

- Clinical Quality Management Plan (CQMP): A clinical quality management plan is a written document that encompasses both quality assurance and quality control procedures and details the responsibility, scope, and frequency of these activities. A CQMP is designed to assess the site performance of clinical research.
- Corrective Action Plan (CAP): A corrective action plan is a written document that details the implementation of actions taken to detect and eliminate the cause of an area of non-compliance, and prevents reoccurrence of non-compliance.
- Key Quality Indicator (KQI): Key quality indicators are selected performance areas and activities that are vital to compliance with accepted standards of performance. For example, verify for eligibility and proper implementation of the informed consent process.
- Quality Assurance (QA): Quality assurance is the periodic, systematic, objective and comprehensive examination of the total work effort to determine the level of compliance with accepted Good Clinical Practice standards. For example, a monthly review of source documents compared to case report form (CRF) pages determine adherence to protocol requirements.
- Quality Audit: An evaluative process for determining the compliance and/or effectiveness of a process or system. A quality audit is a positive and constructive process intended to identify the activities apt to create problems.
- Quality Control (QC): Quality control is the real time ("day-to-day") observation and documentation of the site's work processes to ensure that accepted procedures are followed. For example, review of demographic information for accuracy on each case report form (CRF) prior to entry into a database.
- Quality Management (QM): Quality management is the overall system that includes all activities involved in Quality Assurance and Quality Control, including the assignment of roles and responsibilities, the reporting of results, and the resolution of issues identified during the review.
- Root Cause Analysis: The process for identifying the most basic or causal factor(s) of a problem, inadequate performance, or an obstacle to improvement exists.
- Sample Size: Sample size is the quantitative selection of items or units (records) from a total population for review.

5.0 Responsibilities

Role	Responsibility
Division of Microbiology and Infectious Diseases (DMID)	• Notifies Principal Investigators of their responsibility for CQMP development, implementation and evaluation. • Reviews *findings* from CQMP activities, as applicable.
Clinical Research Site Principal Investigator (PI), or designee Clinical Research staff	• Develops, implements and evaluates the CQMP. • Conducts internal quality management activities, including corrective and preventive actions. • Provides a written CQMP to DMID, upon request. • Reviews CQMP, annually. • Submits revisions to DMID for review and acceptance as appropriate or requested.
Office of Clinical Research Affairs (OCRA)	• Reviews and accepts site/protocol-specific CQMP for

	protocols with an assigned Medical Monitor.
DMID Clinical Trials Management contractor	• Assists DMID with review of and recommendations for CQMP plans submitted by DMID-supported clinical research sites.

6.0 Policy Implementation

DMID requires clinical research sites to develop, implement, and evaluate a CQMP.

6.1 Clinical Quality Management Plan Basic Requirements

6.1.1 Plan Type: Site or Protocol Identification

6.1.1.1 Include Site name

6.1.1.2 Include protocol title and number (if protocol-specific plan)

6.1.1.2.1 Version control: include version number and/or date to correspond with a specific CQMP and associated tools.

6.1.2 Responsibility

6.1.2.1 Name the person(s) responsible for the development, implementation, and evaluation of the CQMP.

6.1.3 **Quality Management Process Description** – The CQMP describes the quality assurance and quality control activities conducted at the site or per the protocol. Sample quality management tools are provided by DMID and available for use.

6.1.3.1 Quality Assurance (QA) – The quality assurance process determines the type and accuracy of the data reviewed by assessment of the key quality indicators (Section 6.1.4).

6.1.3.2 Quality Control (QC) –The quality control activity is an ongoing day-to-day review of 100% of all data collection forms for completeness, accuracy and logic.

6.1.3.3 Record Selection – The clinical research site determines when reviews occur and the minimum percentage of records to be reviewed based on, but not limited to new protocols, initial enrollment, protocols involving study product and/or a procedure, and new clinical research staff. Records include, but are not limited to, case report forms (paper and electronic CRFs), clinical laboratory reports, specimen logs, clinic notes, subject charts, and other source documents.

6.1.4 **Key Quality Indicators –** The following key quality indicators, as applicable, could be audited in each subject record selected for review. A Sample Chart Audit Tool is provided by DMID and available for use.

6.1.4.1 Informed consent form and process

6.1.4.2 Eligibility criteria

6.1.4.3 Study product preparation, administration, and accountability. The CQMP describes the periodic QM activities that are performed in accordance with the ICH Guidelines for Good Clinical Practice; E6, Section 4.6 Investigational Product(s), and applicable regulatory requirements, addressing study product accountability, management and protection of human subjects. Blind for study product must be maintained during internal review of these documents and systems. Study product review activities may include, as applicable, but are not limited to the following:

6.1.4.3.1 Review and comparison of the study product accountability logs, shipping records, and the study product inventory

6.1.4.3.2 Randomization code list and decoding procedures

6.1.4.3.3 Study product storage, handling, and labeling procedures

6.1.4.3.4 Vaccine or other study product preparation procedures

6.1.4.3.5 Study product administration processes

6.1.4.4 AE/SAE identification and reporting

6.1.4.5 Protocol Visits

6.1.4.6 Protocol-specific procedures

6.1.4.7 Intervention/study discontinuation

6.1.4.8 Reactogenicity

6.1.4.9 Specimens (processing, storage, documentation)

6.1.4.10 Other protocol-specific indicators, as determined by the site staff.

6.1.5 **Regulatory File Review** – Regulatory file review is performed, once during the active study period, or annually. A sample Regulatory File Review Tool is provided by DMID and available for use.

6.1.6 **Tools, Checklists, and Reminders –** The CQMP describes the types of tools, checklists, and reminders used during the QM process. Examples may include, but are not limited to, the following:

6.1.6.1 Internal (site) sources:

6.1.6.1.1 Visit reminder checklists, chart audit worksheets/tools (Sample Chart Audit Tool)

6.1.6.1.2 Regulatory File Review Tool (Sample Regulatory File Review Tool)

6.1.6.1.3 Summary Reports from Internal QA/QC Findings (Sample Quality Management Summary Report Tool)

6.1.6.2 External sources:

6.1.6.2.1 Data Entry, query/error, or transmission Reports from the Data Management Center

6.1.6.2.2 Clinical Site Monitoring Reports

6.1.6.3 Other QA/QC Forms

6.1.7 **Staff Training/Qualifications –** The CQMP describes the processes for ensuring and documenting qualified personnel. Examples may include, but are not limited to the following:

6.1.7.1 Institution-Specific Training (i.e., Human Subjects Protection, Phlebotomy, Dangerous Goods Regulations, research staff training, applicable site policies/procedures)

6.1.7.2 Protocol-Specific Training (i.e., specimen handling/processing, study product, data management)

6.1.7.3 DMID-Specific Training

6.1.7.3.1 Human Subjects Protection Training (Required)

6.1.7.3.2 Good Clinical Practice Training (Recommended)

6.1.7.3.3 DMID Regulatory File Document Guidelines

6.1.7.3.4 DMID Source Documentation Guidelines

6.1.8 **Quality Management Summary Reports –** The CQMP describes how findings are summarized, analyzed, and communicated to the staff. A sample Quality Management Summary Report tool is available for use. The basic elements of the Summary Report include, but are not limited to, the following:

6.1.8.1 Staff participation in audits

6.1.8.2 Identification of problem areas

6.1.8.3 Trend analysis

6.1.8.4 Corrective action plan(s)

6.1.8.5 Possible need for revision to CQMP

6.2 **CQMP Submission, Review, and Acceptance – Overview**

6.2.1 **Submission:**

6.2.1.1 DMID or its designee may request the PI or their designee to submit a protocol-specific or site CQMP. The CQMP must address the applicable DMID basic requirements as described above. (See Scope, Section 2.0)

6.2.1.2 DMID will query organizations, which provide structure to multiple sites, to submit their CQMP.

6.2.2 **Review:**

6.2.2.1 CQMPs requested by DMID are reviewed against the DMID basic requirements outlined in this policy. This responsibility may be delegated to the DMID Clinical Trials Management (CTM) contractor.

6.2.2.2 DMID will communicate review findings and recommendations to the PI/designee via email within fourteen (14) calendar days.

6.2.3 **Acceptance:**

6.2.3.1 As applicable (see *Review 6.2.2.1*), following resolution of the CQMP review, DMID will provide to the PI/designee a written notification accepting the CQMP.

6.3 **Site Evaluation of the Clinical Quality Management Plan**

6.3.1 DMID recommends the PI/designee document, in the CQMP, plans for evaluating the effectiveness of the CQMP annually, at a minimum. If the CQMP is modified to increase the effectiveness, the submission process is reactivated (See Scope, section 2.0).

7.0 References

7.1 **International Conference on Harmonization (official website)**

7.1.1 Guidelines for Good Clinical Practice (GCP) E6 (R1)

7.2 **Office for Human Research Protections**

7.2.1 Code of Federal Regulations 45 Public Welfare, Department of Health and Human Services Part 46 Protection of Human Subjects

7.2.2 Code of Federal Regulations, Title 21 (applicable parts 11, 50, 54, 56, 312, 812)

7.3 **Division of Microbiology and Infectious Disease**

7.3.1 Regulatory File Guidelines
7.3.2 Source Documentation Standards
7.3.3 Quality Management Policy, Tools and Guidance

8.0 Inquiries

Questions or comments regarding this policy may be directed to:

Claudia Baxter, RN, BSN
Nurse Consultant
NIH / NIAID
Division of Microbiology and Infectious Diseases (DMID)
Office of Clinical Research Affairs (OCRA)
Bethesda, MD 20892
baxterc@niad.nih.gov

9.0 Availability

This policy, guidance and sample tools are available electronically:

NIAID Internet/DMID/Policies and Procedures
http://www3.niaid.nih.gov/research/resources/DMIDClinRsrch/quality.htm

DMID Clinical Trials Management contractor (PPD)
http://www.dmidctm.com/partners/SectionQualityManagement/PageSOPs/SOPs.htm

An original signed approval is located within the OCRA Clinical Trials Management Section (CTMS)

office.

10. Change Summary

Version Number:	Date of Revision: DD/MMM/YYYY	Replaces:	Effective Date: DD/MMM/YYYY	Description of Revision/Retirement:	Revision Initiated by:
1.0	N/A	N/A	14-Jan-2008	N/A	N/A
2.0	18/AUG/2008	1.0	1-Sept-2008	Update links, clarify purpose, workflow, administrative corrections	DMID Policy Development Team
3.0	23/FEB/2009	2.0	1-Apr-2009	Add KQI, clarifying language; sample tools revised	DMID Policy Development Team

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